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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/253,573	02/19/1999	HAI XING CHEN	99.001	5784

7590 12/17/2002

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EXAMINER
SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/253,573	Chen
Examiner	**Art Unit**
Richard Schnizer	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Nov 15, 2002* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *Nov 15, 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see NOTE below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: *1, 2, 6-8, 11, 12, and 14*

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .

10. ☐ Other:

ADVISORY ACTION

The request for reconsideration does not place the application in condition for allowance.

The claimed invention is a method for producing and delivering protein *in vivo*. Claims 1, 2, 6-8, 11, 12, and 14 embrace methods of delivering to progenitors of mammalian red blood cells isolated from a mammalian host an expression construct comprising a promoter operably linked to a gene encoding a protein which is not native to red blood cells. The transfected progenitors are then reintroduced into the mammalian host, wherein they give rise to red blood cells containing the desired protein. The red blood cells subsequently lyse, resulting in delivery of the protein.

The claims stand rejected for lack of enablement because the specification asserts no use for the claimed invention other than gene therapy, and discusses the claimed invention only in the context of gene therapy.

At page 4 of the response, Applicant reiterates the position that the claimed invention is a method of in vivo protein production and delivery, asserting that although the invention may be used for disease treatment, it is not intended to be a specific gene therapy protocol. This raises the question of for what, other than gene therapy, the invention is intended to be used. At page 7 of the response Applicant argues that the specification teaches a host of utilities, citing page 6 of the specification. The cited utilities include "a non-tissue specific method for the synthesis of proteins; a means to control the expression and production of proteins in the precursors of red

blood cells; taking advantage of the lack of a nucleus in a red blood cell to provide enhanced stability of proteins after their production; and bypassing exocytosis and secretion pathways for protein release. None of these utilities provides reason for the *in vivo* production and delivery of proteins as claimed. The Examiner has carefully read the specification and found that, as stated in the rejection above, the specification asserts no use for the production and delivery of proteins in vivo other than therapy. Because of this, in order to adequately teach how to use the invention for the only purpose for which the specification teaches it was intended, the specification must enable the practice of gene therapy of the broad range of diseases set forth in the specification. Applicant has failed to point to any support in the specification for the use of the invention for any purpose other than gene therapy.

At page 5 of the response, Applicant argues that the Examiner has failed to point out any particular claim elements that are broader than a method for producing protein only in the progenitor cells of red blood cells such that the claims are not enabled. Applicant also argues that the Examiner has failed to point out any inconsistency in the plain meaning of the claim terms to indicate that the claim terms are broader than a method of producing protein such that the claims are not enabled. These arguments are unpersuasive. AS noted above and in Papers 14 and 17, the specification must teach how to make and use the invention as intended. The only purpose for expressing proteins in vivo set forth in the specification is the therapy of diseases. Applicant has failed to point to any other purpose for expressing proteins in vivo. The Office must consider

enablement in view of the intended use of the invention. The specification fails to enable methods of therapy for the reasons set forth in Paper Nos. 14 and 17.

At page 6-8 of the response, Applicant continues to argue that gene therapy is a separate invention which need not be enabled. In response, the Office reiterates that Applicant must teach how to use the invention for the purpose for which it was intended to be used. The specification discloses no use for the invention other than gene therapy, so in order to enable the claimed invention the specification must teach how to perform gene therapy. It does not, for the reasons set forth previously in Paper Nos. 14 and 17. Applicant further argues the specification is enabling in the same way that Hollis is enabling, i.e. Hollis teaches the non-therapeutic utility of production and purification of recombinant proteins, whereas the instant specification teaches the production of and delivery of proteins in vivo. This is unpersuasive because there are clearly a variety of uses for purified proteins known to those of skill in the art. Applicant has failed to point to any purpose for production and delivery in vivo other than therapy, and the specification fails to teach one. For this reason, the claims read on protein expression and delivery for therapy.

At page 8, Applicant argues that, "recent advances in gene therapy", gene therapy is a feasible approach for medical treatment of diseases, and it should be understood that while the claimed inventions can be a method of delivering a protein for a gene therapy protocol, it is separate and distinct from gene therapy. In response, the Office notes that the invention is not separate from gene therapy because the specification teaches no other purpose for it. Regarding

the relevance of Exhibit A to the state of the art of gene therapy, Applicant is reminded that developments occurring after the filing date of an application are of no significance regarding what one skilled in the art believed as of that filing date. See for example, *in re Wright*, 27 USPQ2d 1510, 1514 (Fed. Cir. 1993).

At page 9, Applicant argues that it would be unjust to require applicant to delay seeking patent protection on a mechanism of protein delivery until after "the specific gene therapy has been discovered and proven." This is unpersuasive for the reasons set forth above, i.e. enablement of the claims depends on whether the specification teaches how to make and use the invention. In this case the only asserted use of the invention is in gene therapy. For this reason, the specification must enable the use of the invention in gene therapy. The specification fails to do this for the reasons given above.

JEFFREY SIEW
PRIMARY EXAMINER
12/13/02